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Comparison of the Adjunctive Effect of Tranexamic Acid and Infusion Oxytocin on Blood Loss at Caesarean Section - A Randomised Study

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Abstract
Background: *Postpartum haemorrhage is a major complication at caesarean section. Tranexamic acid and oxytocin infusion have been used for prophylaxis.*
Aim: *To compare the effectiveness of prophylactic adjunctive use of Tranexamic acid and oxytocin infusion at caesarean section to reduce blood loss.*
Method: *A randomised study at ABUTH, Zaria, in which 144 women, scheduled for elective or emergency caesarean section at term, were sequentially randomised into two groups of 72 each. The Tranexamic acid group received 1g intravenous and 500ml of Normal saline as placebo while the oxytocin group received placebo and 500ml of Normal saline containing 20IU of oxytocin after delivery of the neonate. Both adjunctive groups received 10IU Oxytocin as part of AMTSL. Trial registry: PACTR 202004568331645. Ethical approval: ABUTHZ/HREC/D37/2018.*
Result: *There was no significant difference in parity, gestational age and indication for caesarean section in both groups p<0.287, 0.270 and 0.095 respectively. There was no significant difference in primary outcome with mean blood loss 561.06 ± 209.23ml versus 567.78 ± 205.91ml in the Tranexamic acid and oxytocin group respectively, p<0.847. Need for additional uterotonic agent and side effect profile were significantly reduced in the Tranexamic acid group. There was no significant difference in need for blood transfusion and haemodynamic status of parturient in both groups. There was no significant difference in mean blood loss at emergency versus elective caeserean section, 565.83± 205.51ml versus 567.97± 217.42ml respectively, p<0.921.Blood loss in those with 1 previous CS was comparable in both groups 537.75± 209.69ml versus 522.05± 176.43ml respectively, p<0.374, however, for those with 2 or more CS, while there was a clinical (reduction) difference of 80ml in the Tranexamic acid group, it was not statistically significant. 594.55± 0.91ml versus 674.06± 1.99ml respectively, p<0.476.*
Conclusion: *There is comparative adjunctive efficacy of Tranexamic acid and oxytocin infusion at caesarean section.*
Keywords: *Caesarean delivery, Oxytocin infusion, Tranexamic acid, Postpartum haemorrhage.*

Introduction

Despite the progress made in recent years in reducing the number of women who suffer morbidity and mortality from postpartum haemorrhage (PPH), it still remains the most common direct cause of maternal death in low-income countries.[1] Postpartum haemorrhage is more common after caesarean section than after vaginal delivery.[2] Reducing blood loss during and after caesarean section has been shown to directly improve the outcome.[3]

Utero-tonics are routinely used at caesarean section, to reduce blood loss and the risk of postpartum haemorrhage and Oxytocin remains the first-line agent for the prevention and treatment of uterine atony.[4] The approach of using oxytocin infusion, reflects concerns about the physiological effects of bolus oxytocin.[5] Intravenous oxytocin has a short half-life (4-10minutes), therefore, the potential advantage of an oxytocin infusion at caesarean section is in maintaining uterine contractility throughout the surgical procedure, and the immediate postpartum period, when most primary postpartum haemorrhage occurs.[6]

Pro-haemostatic drugs such as tranexamic acid (TXA), provide complementary biochemical haemostatic effects, to the well-proven utero-tonics, especially oxytocin.[7] Tranexamic acid is a potent anti-fibrinolytic agent that exerts its effect by blocking lysine binding sites on plasminogen molecule and has the potential to enhance the effectiveness of the patients own haemostatic mechanisms, consequently, clot breakdown (fibrinolysis) is inhibited and bleeding is reduced.[8]

A study by Lakshimi and Abraham on the role of prophylactic tranexamic acid, in reducing blood loss during caesarean section, a randomized controlled study involving 120 women, found TXA significantly reduced the amount of blood loss during lower segment caesarean section (LSCS).[7] Gongorduk and fellow workers in their study on the efficacy and safety of tranexamic acid in reducing blood loss during elective section, randomized 660 parturient in a randomized double blind placebo controlled trial, found the estimated mean blood loss was lower in tranexamic acid group compared with women in the placebo group (499.9±206.4ml versus 600.7±215.7ml, respectively; $p<0.001$).[9]

A study by Obi and colleagues in Abakaliki on the efficacy of intravenous tranexamic acid on reduction of blood loss at caesarean section found that estimated blood loss was significantly lower in the tranexamic acid group (566.7ml versus 819.09ml. $p <0.001$).[10] Ahmed et al, in their work evaluated 124 women randomized to receive 10mg/kg of tranexamic acid intravenously 5minutes before skin incision while the control group did not. Both groups received 10IU of oxytocin and 1ml of ergometrine after delivery of the fetus. Their findings showed lower amount of blood loss (391ml) in the tranexamic acid group compared to the control group (597ml).[11]

Abdel-Aleem and co-workers, in their study on the effectiveness of tranexamic acid on blood loss in patients undergoing elective caesarean section, randomized 740 eligible women to receive either 1g tranexamic acid or nothing. All women received 5IU of oxytocin bolus and 20IU in intravenous infusion. Their conclusion was in keeping with others that tranexamic acid significantly reduced blood loss in the study (tranexamic acid) group.[12]

A study by Kazume et al, on the routine use of prophylactic oxytocin in the third stage of labour found, that it efficiently reduced the volume of blood loss and the incidence of PPH without significant increase in the incidence of adverse outcome.[13] Adanikin and fellow researchers compared oxytocin infusion to rectal misoprostol in preventing postpartum haemorrhage after caesarean section.[14] In this study, fifty pregnant women were randomized to receive 600ug rectal misoprostol and 20IU oxytocin infusion. Findings from the study showed that blood loss was not significantly different between the rectal misoprostol and oxytocin infusion group.

Aims

To compare the effectiveness of the adjunctive use of tranexamic acid and oxytocin infusion in reducing blood loss at caesarean section.

Specific Objectives

1. To determine if there is a difference in mean blood loss and haemoglobin concentration in both arms of the study.
2. To determine the incidence of postpartum haemorrhage in both arms of the study.
3. To determine the proportion of patients who had blood transfusion in the TXA and oxytocin infusion arms of the study.
4. To determine the need for medical and surgical intervention in both arms of the study.
5. To determine the side effects and haemo-dynamic changes during the operation in both arms of the study

Test of Hypothesis

Null hypothesis H_o = There is no difference between intravenous tranexamic acid and oxytocin infusion when used adjunctively for the reduction of blood loss at caesarean section.

Alternate hypothesis H_A = There is a difference between intravenous tranexamic acid and oxytocin infusion when used adjunctively for the reduction of blood loss at caesarean section.

Methodology

Study Design: The study was a prospective randomized study.

Study Setting: The study was carried out at the Ahmadu Bello University Teaching Hospital (ABUTH) Zaria.

Study Population

Consenting women scheduled for elective or emergency caesarean delivery under regional anaesthesia at ABUTH, who met the inclusion criteria.

Inclusion Criteria

Women with singleton pregnancy at gestational age >37 weeks.

Exclusion Criteria

Outlined in the protocol chart below

Sample size determination

Sample size was calculated using the formula: [15]

$$\text{Sample size (n)} = \frac{2SD^2(Z_{a/2} + Z_B)^2}{d^2}$$

SD = Standard deviation from previous study

$Z_{a/2} = Z_{0.05/2} = Z_{0.025} = 1.96$ (from Z table at type 1 error of 5%)

$Z_B = Z_{0.80} = 0.842$ (from Z table) at 80% power

d= effect size = difference between mean values

The study on prophylactic tranexamic acid by Laskshimi et al,[13] found mean blood loss of 347.17ml in the study group, and 517.72ml in the control group. The power of this study will be set at 80% and two sided confidence interval at 95%.

$$\text{Sample size (n)} = \frac{2SD^2 (Z_{a/2} + Z_B)^2}{d^2}$$

SD= 347.17

$Z_{a/2}$= 1.96, Z_B = 0.842

d= 517.72 – 347.17ml = 170.55

$$n = \frac{2 \times (347.17)^2 (1.96 + 0.842)^2}{170.55^2}$$

n = 65.064

With calculation of 10% attrition rate, 72 patients were recruited in each group with a total of 144 eligible women.

Study Protocol

Patient Enrolment

As parturients presented for elective or were planned for emergency caesarean section, their history were comprehensively reviewed by a research assistant. Those that met the inclusion criteria and consent were enrolled into the study. Their vital signs were recorded and pre-operative haemoglobin estimated.

Randomization Technique

This was done using the basic steps in a randomization process.

Sequence generation: A computer generated random number chart of 144 numbers and study category, was prepared by a research assistant who was not involved in the study. A print of the randomization chart was kept in a secured place in the delivery suite. It depicted the random number alongside the groups of either A or B against each number.

Allocation concealment was done sequentially. One hundred and forty four (144) sealed opaque envelopes each containing a piece of paper with a random number from 001-144 was prepared by a research assistant. The envelope being opaque prevented its contents being seen by the patient or the primary investigator thus preventing selection bias. The sealed envelope was put in a box kept secured and inaccessible to the primary researcher and others in the theatre.

Allocation: The numbers 001-144 was allocated to two groups. Group A (72 numbers) was the Tranexamic acid group and group B (72 numbers) was the oxytocin group.

Study protocol:

Group A: 1g Tranexamic acid (Tranexamic acid injection ®;Vital Healthcare India) diluted up to 50ml with sterile water was administered atleast 30 minutes before surgery + 500ml Normal saline as placebo after delivery of neonate.

Group B: 50ml sterile water as placebo + 500ml of Normal saline containing 20IU of oxytocin (Oxytocin®; RotexMedica Germany) after delivery of neonate.

Protocol Implementation

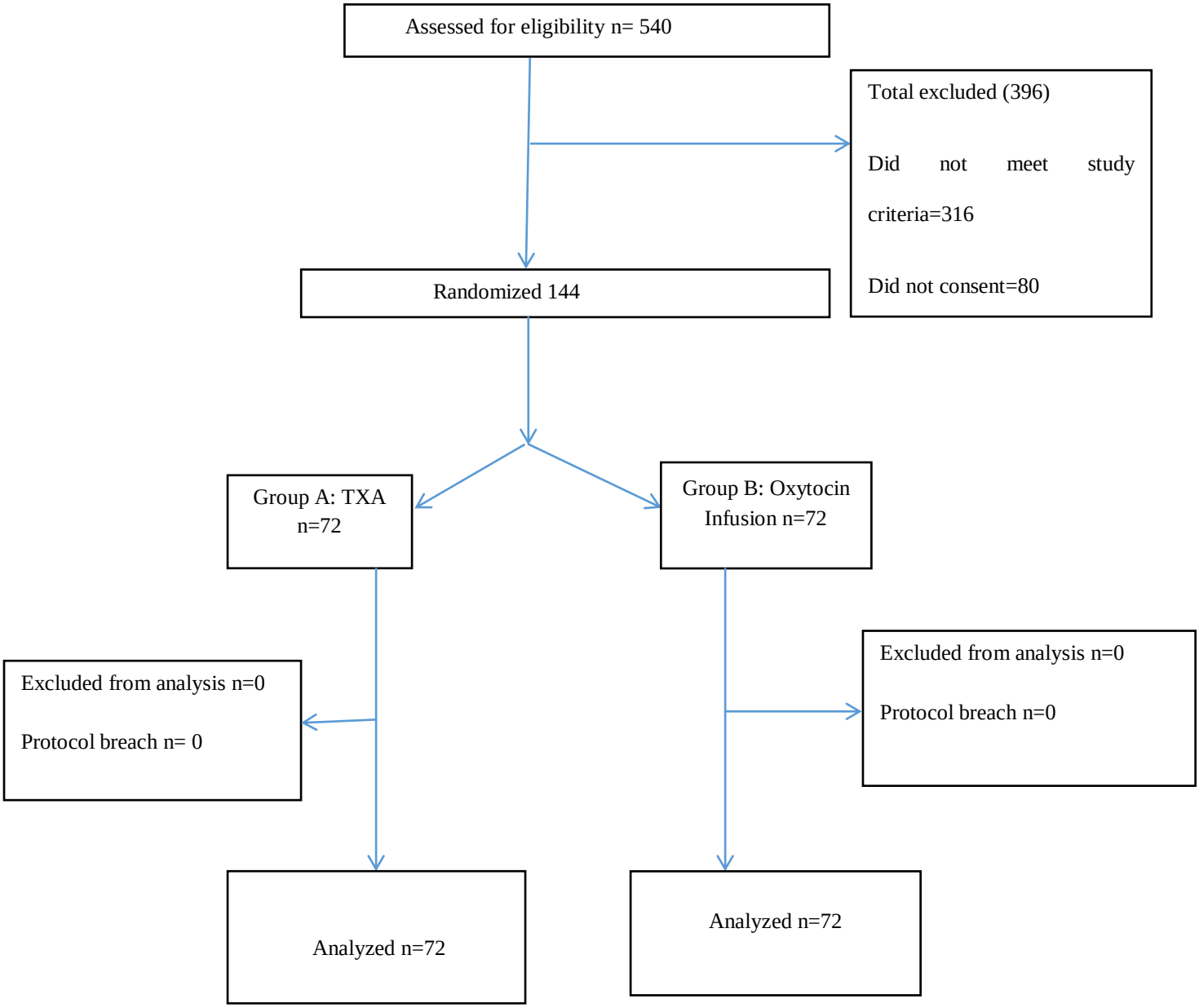
Following counselling and informed consent, patients were asked by a research assistant to pick one of the sealed opaque envelopes. The assistant then opened the envelope to retrieve the piece of paper inside it and check the number on it. This number was then checked on the chart of computer generated random numbers to know the group a participant fell into- group A or B. Patients were allocated to the group which their number appeared on the chart. At the waiting area of the theatre, patients in group A received intravenous 1g TXA diluted up to 50 ml with sterile water and administered slowly over 10 minutes , atleast 30 minutes before skin incision, while patient in group B, received 50ml of placebo (sterile water), slowly over 10 minutes at least 30 minutes before skin incision. This was only known by the randomizing research assistant, who recorded it and handed the 500ml Normal saline infusion to the anaesthesiologist while he/she left the theatre temporarily.

The 500ml Normal saline infusion were commenced immediately following delivery of the neonate. Following the delivery, 10 IU bolus intravenous oxytocin was given slowly to both group of women. The Normal saline infusion was set up to flow over 4hour at 125ml/h. For patient in group A, it was plain, while for patients in group B, it contained 20IU of oxytocin.

The outcome was assessed by the primary researcher, who filled the outcome in the proforma and dropped it in an outcome envelop. The research assistant who randomized, then returned to the theatre at the end of the surgery and picked up the proforma in the outcome envelop and indicated the study group in the proforma (which hither to, had not been indicated) and was in custody of the filled proformas until the end of the study. The patient and primary researcher were blinded to the study group.

Spinal anaesthesia and caesarean section was carried out by senior doctors, from the cadre of senior registrar and consultants following standard protocols. Blood loss was measured from placental delivery till the end of the surgery by measuring blood collected in a dedicated, study suction bottle; soaked swabs, mops and operation table perineal sheet and pads, which are pre-weighed before the surgery. Blood collected prior to placental delivery and liquor, was collected in a separate suction container. All blood loss before placental delivery was not included in the study.

Figure 1. Study Flow Diagram



Quality Control and Assurance

A research assistant was designated for this purpose, to carry out a survey on the effectiveness and success of the blinding by asking a sub-sample of 36 women in each group, the primary researcher, the surgeons and anaesthesiologist in each case on the likely study group a patient belongs. The blood loss assessment was mostly carried out by the primary researcher. Different research assistants were involved at various stages of the study. These measures maintained consistency and limited confounding variables.

Study Outcome

Primary outcome:

- Difference in mean blood loss between both arms of the study

Secondary outcomes:

- Incidence of postpartum haemorrhage in both arms of the study.
- Incidences of greater than 10% fall in haemoglobin concentration in both arms of the study.
- Proportion of women in both arms who require medical and surgical interventions.

- Proportion of women who need blood transfusion in both arms of the study.
- The proportion of women with haemodynamic instability and adverse drug effects.

Data Analysis

Data obtained was analysed using IBM statistics data editor SPSS version 21. Categorical data were expressed as frequencies and percentages. Mean and standard deviation were calculated for age, gestation age and amount of blood loss. Unpaired t-test were used to find the significance between the two groups with regards to continuous variables. Chi test were used to find significance in the incidence of increased blood loss (greater than 1000ml) and the incidence of greater than 10% fall in hemoglobin in both groups. Probability value of $P \leq 0.05$ was taken as the level of significance.

Ethical Considerations

Ethical approval was obtained from the ABUTH Research Ethics Committee: ABUTHZ/HREC/D37/2018. The study was registered at the Pan African Clinical Trial Registry: PACTR 202004568331645.

Results

This study was conducted from February 2019 to July 2019. One hundred and forty four patients were recruited for the study.

Table 1: Baseline characteristics

	Group A (n=72)	Group B (n=72)	P -value
Mean Age (years)	28.17 ± 6.64	30.56 ± 6.03	0.012
Parity	2.56 ± 2.71	2.29 ± 2.03	0.287
Gestational Age (weeks)	39.04 ± 1.60	37.98 ± 4.84	0.270
Booking Status			0.405
Booked	49 (68.1%)	61 (84.7%)	
Unbooked	22 (30.6%)	11 (15.3%)	

Table 1 reveals the baseline characteristics of the groups. There was no significant difference in these characteristics apart from the age in both groups.

Table 2: Table 2: Indication for caesarean section

	Group A n (%)	Group B n (%)	P -values
1 Previous CS	20 (27.8%)	17 (23.6%)	0.095
2 Previous CS	11 (15.3%)	16 (22.2%)	
Fetal distress	3 (4.2%)	9 (12.5%)	
Obstructed Labour	6 (8.3%)	3 (4.2%)	
Prolonged Labour	5 (6.9%)	4 (5.6%)	
Non reassuring CTG/BPP	1 (1.4%)	11 (15.3%)	
Others	26 (36.1%)	12 (16.7%)	

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Table 2 shows the indications for the caesarean section in both groups

Table 3: Mean Blood loss Estimation and Significance in both Groups (primary outcome)

Blood loss (mls)	Mean ± SD	t- value	P –value
Group A	561.06 ± 209.23	-0.194	0.847
Group B	567.78 ± 205.91		

Table 3. There was no significant difference in the primary outcome: mean blood loss.

For the secondary outcomes: mean difference in haemoglobin concentration and >10% fall in haemoglobin, incidence of PPH and need for blood transfusion, table 4,5,6,7,8,9 and 10 demonstrates that there was no significant difference but for need of additional uterotonic agents which was significantly less in the TXA group (p value = 0.036; OR 0.474).

Table 4: Haemoglobin Estimation and Significance in both Groups

Hb Concentration.		Mean ± SD	95% CI (Lower - Upper)	t-value	P -value
Hb. before Delivery			-0.870 - 0.073	-1.672	0.097
	Group A	11.23±1.71			
	Group B	11.63±1.09			
Hb. after Delivery			-0.750 - 0.184	-1.199	0.232
	Group A	9.84±1.52			
	Group B	10.13±1.30			

Table 5: Mean difference in haemoglobin concentration

Mean HB Difference	Mean ± SD	t-value	P –value
Group A	1.37 ± 0.87	-1.469	0.144
Group B	1.68 ± 1.59		

Table 6: Percentage fall in haemoglobin concentration

% Hb fall	Group A	Group B	Total	x^2	P -value	OR
< 10% fall	31 (43.1%)	31 (43.1%)	62 (43.1%)	0.000	1.000	1.000(0.517-1.934)
> 10% fall	41 (56.9%)	41 (56.9%)	82 (56.9%)			
Total	72(100.0%)	72 (100.0%)	144(100.0%)			

Table7: Blood loss estimation and significance in both groups

Blood loss	Group A	Group B	Total	x^2	P -value
≤ 499mls n (%)	31 (43.1%)	27 (37.5%)	58 (40.3%)	0.700	0.705
≥500ml-999ml n(%)	35 (48.6%)	40 (55.6%)	75 (52.1%)		
≥1000ml n(%)	6 (8.3%)	5 (6.9%)	11 (7.6%)		
Total	72 (100.0%)	72(100.0%)	144(100.0%)		

Table 8: Blood loss estimation and significance in both groups

Bloodloss n(%)	Group A	Group B	Total	x^2	P-value	OR
<1000mls	66 (91.7%)	67 (93.1%)	133 (92.4%)	0.098	0.754	0.821(0.239-2.821)
≥1000ml	6 (8.3%)	5 (6.9%)	11 (7.6%)			
Total	72(100.0%)	72(100.0%)	144(100.0%)			

Table 9: Need for blood transfusion in the groups

Blood Transfusion n(%)	Group A	Group B	Total	x^2	P-value	OR
Transfused	13 (18.1%)	16 (22.2%)	29 (20.1%)	0.389	0.533	0.771(0.340-1.748)
Not Transfused	59 (81.9%)	56 (77.8%)	115(79.9%)			
Total	72 100.0%)	72 100.0%)	144(100.0%)			

Table 10: Need for additional Uterotonics in both groups

Uterotonics	Group A	Group B	Total	x^2	P-value	OR
Needed n(%)	19 (26.4%)	31 (43.1%)	50 (34.7%)	4.412	0.036	0.474(0.235-0.956)
No need n(%)	53 (73.6%)	41 (56.9%)	94 (65.3)			
Total	72 100.0%)	72 (100.0%)	144(100.0%)			

Table 11. There was significant reduction in the side effect profile in the tranexamic acid group (p value = 0.037).

Table 11: Adverse Effects in the Groups

Adverse Effects	Group A n (%)	Group B n (%)	Chi-Square (x^2)	p-value
None	62 (86.1%)	48 (66.7%)	8.457	0.037
Nausea	6 (8.3%)	15 (20.8%)		
Vomiting	4 (5.6%)	7 (9.7%)		
Others	0 (0.0%)	2 (2.8%)		

There was no thromboembolism reported in both group and no maternal death. Also no patient had need for any obstetric manoeuvre in the theatre

Table 12: Maternal vital signs

	Group A	Group B	p-value
PULSE RATE			
At skin incision	97.74±12.43	94.25±15.78	0.315
30min intra-op	99.97±13.56	97.67±13.26	0.478
1 hour post-op	97.77±16.05	96.21±14.34	0.675
24 hour post-op	95.13±12.97	90.43±13.62	0.156
SYSTOLIC BP			
At skin incision	121.97±21.94	123.95±24.49	0.727
30min intra-op	117.55±20.98	118.00±19.34	0.926
1 hour post-op	121.93±17.70	119.03±16.43	0.483
24 hour post-op	124.13±16.11	122.11±21.43	0.670
DIASTOLIC BP			
At skin incision	73.32 ±19.86	74.45±19.74	0.815
30min intra-op	68.74±19.81	69.08±14.98	0.936
1 hour post-op	65.80±11.57	67.15±11.22	0.626
24 hour post-op	69.57±12.65	68.79±13.23	0.807
MAP			
At skin incision	88.62±16.03	84.46± 18.28	0.337
30min intra-op	83.69±15.43	84.95±12.91	0.720
1 hour post-op	86.18±11.25	86.95±13.04	0.804
24 hour post-op	88.89±12.95	89.23± 14.95	0.925

There was no change in haemodynamic status as demonstrated by the vital signs at skin incision, 30 minutes intra-operatively, 1 hour intra-operatively and 24hour intra-operatively.

Discussion

There was no significant difference in the primary outcome with mean blood loss of 561.06 ± 209.23ml in the tranexamic acid group and 567.78 ± 205.91ml in the oxytocin group p<0.847. The findings agrees with report by Obi et al,[10] which found a mean blood loss in the tranexamic acid group to be 566.78ml±267.42ml and that compared to placebo it significantly reduced blood loss. However, that study compared tranexamic acid with placebo and oxytocin was only used when indicated. The work of Roy et al,[16] from India with blood loss of 558mls agree with the study findings, which is at variance with the findings of reduced blood loss in the tranexamic acid group (241 - 499ml) by Lakshimi et al,[7] Movafegh et al,[15] Ahmed et al[11] , Abdel-Aleem,[12] and Thavare et al.[17] The mean blood loss in the oxytocin infusion group agrees with findings by Thavare et al[17] which found a mean blood loss of 576ml.± 06ml in their oxytocin group which also received 20IU oxytocin in 500ml saline after neonatal delivery. It is also consistent with the findings from the placebo group in the study by Lakshimi and colleagues[7] in which an oxytocin infusion of 10IU/l was used with a mean blood loss of 517.72±150ml. The findings is however different from findings of Roy et al,[16] who reported with a mean blood loss of 800.91 ml despite, a maintenance oxytocin of 10IU in 500ml of normal saline in the placebo group.

Our study also found that, on the secondary outcomes, there was no significant difference in the incidence of PPH in both groups with 8.3% in the TXA group and 6.9% in the oxytocin group p= 0.705. This incidence of PPH is in consonance with the findings by Obi et al[10] of 8.8% in the TXA group versus 27.6% in the placebo group. However the finding is at variance from the study by Roy et al,[16] which found no incidence of PPH in the tranexamic acid group and 12% in the placebo group that received infusion oxytocin.

The mean haemoglobin difference between the group is also not statistically different with 1.37 ± 0.87 in tranexamic acid group and 1.68 ±1.59 in the oxytocin infusion group, p= 0.144. This is in agreement with finding by Bhatia et al,[18] however varies with findings by Obi et al,[10] Roy et al,[16] Ahmed et al,[11] and Abdel-Aleem[12] et al. There was also no statistical difference in the incidence of blood loss >10% fall in Hb levels (56.9%) in both group. This is different from the finding of Lakshimi[10] which showed a significant drop 9.3% versus 39%.

There was however significant difference in the need for additional uterotonic agent between the groups with significant reduction in the tranexamic acid group, 26.4% compared to 43.1% p=0.036. This is similar to findings by Obi et al,[10] Ahmed et al,[11] Gongorduk et al,[9] Lakshimi et al[10] and Movafegh et al.[15]

There was no statistical difference between the groups on the need for blood transfusion 18.1% in the TXA group and 22.1% in the oxytocin infusion group. Even though there was a reduction in the TXA group, this was also not statistically significant. This is similar to findings by Obi et al,[10] Gongorduk et al,[9] which also found no significant difference, but is at variance with findings of Wang and fellow workers.

Although there was no statistical difference in maternal vital signs, there was significant difference in side effect particularly nausea and vomiting p< 0.037 with less in the tranexamic acid group. This is at variance with finding by obi et al, Abdel-Aleem et al, [12] who reported more side effects in the tranexamic acid group and Bhatia et al, Roy et al, [16] Lakshimi[7] which reported no side effects. These differences may be because of the dose and flow rate of the oxytocin infusion. There was no incidence of thromboembolism and no maternal death.

Conclusion

This study demonstrated that pre-operative intravenous tranexamic acid is as effective as

oxytocin infusion commenced after delivery, for the prevention of primary postpartum haemorrhage at caesarean section.

Conflict of Interest

The authors had no conflict of interest

Funding: The authors received no financial support for this work.

Dedication

This work is dedicated to the memory of one of the authors, Late **Prof Marliyya S Zayyan**, an obstetrician and gynaecologist per excellence, who is no longer with us to see the publication.

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HEALTH RESEARCH ETHICS COMMITTEE

AHMADU BELLO UNIVERSITY TEACHING HOSPITAL SHIKA,
ZARIA, NIGERIA.

E- mail: abuthshika@yahoo.com website: www.abuth.org

Chief Medical Director: Prof. Lawal Khalid, MBBS, FMCS, FWACS, FRCS(ED) mni
Chairman, Medical Advisory Committee: Prof Adamu Ahmed, MBBS, (ABU) LLB (ABU), BL, FWACS, FICS, FACS.
Director of Administration: Alh. Abdulraheem Sallau, BA(Pub. Admin) PGDPA, MPA, (ABU) AHAN, ACIPM.
Ag. Chairperson : HREC Prof Aisha I. Mamman MBBS, FMCPath

NHREC/10/12/2015 27th July, 2018 D-U-N-S NUMBER: 954524802

ABUTH/HREC/CL/05

ABUTH HREC FULL ETHICAL CLEARANCE CERTIFICATE

Comparison of the effect of Prophylactic Interavenous Tranexamic acid to infusion oxytocin as Adjunct to bolus oxytocin on Blood loss a Caesarean Section. A Randomised study

ABUTH Ethics Committee assigned number: - ABUTHZ/HREC/D37/2018

Name of the principal Investigator: - **Dr. Dogbanya Gabriel**
Address of the Principal Investigator: - Dept. of Obstetrics & Gynaecology ABUTH, Zaria.

Date of receipt of valid application: - 13th June, 2018

Date of meeting when final determination On ethical approval was made: - 10th July, 2018

This is to inform you that the research described in the submitted protocol, the consent forms and other participant information materials have been reviewed and ***given full approval by the Health Research Ethics Committee.***

Please note: this approval dates from **27th July, 2018 - 27th July, 2019**

No participant recruitment into this research may be conducted outside these dates.

All informed consent forms in this study must carry the ABUTH HREC number assigned to this research and the duration of ABUTH HREC approval of the study.

This HREC expects that you submit your application as well as an annual report for ethical clearance renewal 3 months prior to expiration of study dates. This is to enable you obtain renewal of your approval and avoid interruption of your research.

If there is delay in starting the research, please inform the ABUTH HREC so that starting dates can be adjusted accordingly.

No changes are permitted in the research without prior approval by ABUTH HREC, except in circumstances outlined in national code for Health Research Ethics: **http://www.nhrec.net.**

ABUTH HREC reserves the right to conduct compliance assessment visits to your research site without prior notification.

for 27/07/2018
Prof. Aisha. I. Mamman ***MBBS, FMCPath***
Chairperson

Pan African Clinical Trials Registry

South African Medical Research Council, South African Cochrane Centre
PO Box 19070, Tygerberg, 7505, South Africa
Telephone: +27 21 938 0506 / +27 21 938 0834 Fax: +27 21 938 0836
Email: pactradmin@mrc.ac.za Website: www.pactr.org

Trial no.:	PACTR202004798040817	Date of Approval:	24/04/2020
Trial Status:	Retrospective registration - This trial was registered after enrolment of the first participant		

TRIAL DESCRIPTION

Public title	Comparison of the Effect of Prophylactic Intravenous Tranexamic Acid to Infusion Oxytocin as Adjuncts to Bolus Oxytocin on Blood Loss at Caesarean Section. A Randomised Study
Official scientific title	Comparison of the Effect of Prophylactic Intravenous Tranexamic Acid to Infusion Oxytocin as Adjuncts to Bolus Oxytocin on Blood Loss at Caesarean Section. A Randomised Study
Brief summary describing the background and objectives of the trial	Background: Postpartum haemorrhage and its attendant morbidity and mortality remains a challenge in our settings in Nigeria and it is a major complication during caesarean section. Tranexamic acid is an anti-fibrinolytic agent whose role in the prevention of excessive blood loss at caesarean section is of interest. Current international guidelines recommend the use of oxytocin for PPH prevention during caesarean section, however there is insufficient evidence regarding the effectiveness of continuous infusion in addition to bolus injection. The study aimed to compare the effectiveness of prophylactic intravenous tranexamic acid given before caesarean section versus oxytocin infusion commenced after neonatal delivery, both as adjunct to bolus oxytocin.
Type of trial	RCT
Acronym (If the trial has an acronym then please provide)	TROXY STUDY
Disease(s) or condition(s) being studied	Obstetrics and Gynecology
Sub-Disease(s) or condition(s) being studied	Fertility-female
Purpose of the trial	Prevention
Anticipated trial start date	01/01/2019
Actual trial start date	31/01/2019
Anticipated date of last follow up	31/07/2019
Actual Last follow-up date	31/07/2019
Anticipated target sample size (number of participants)	144
Actual target sample size (number of participants)	144
Recruitment status	Completed
Publication URL	

Secondary Ids	Issuing authority/Trial register

STUDY DESIGN

Intervention assignment	Allocation to intervention	If randomised, describe how the allocation sequence was generated	Describe how the allocation sequence/code was concealed from the person allocating the participants to the intervention arms	Masking	If masking / blinding was used
Parallel: different groups receive different interventions at same time during study	Randomised	Simple randomization using a randomization table created by a computer software program	Sealed opaque envelopes	Masking/ blinding used	Outcome Assessors, Participants